



PHYSICIAN'S ORDER SHEET
STANDING ORDERS FOR:
DROTRECOGIN ALPHA
(XIGRIS®) PROTOCOL

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ANOTHER BRAND OF GENERICALLY EQUIVALENT PRODUCT, APPROVED BY THE PHARMACY AND THERAPEUTICS COMMITTEE, MAY BE ADMINISTERED UNLESS (SPECIFIC) IS WRITTEN AFTER THE MEDICATION ORDER.

DROTRECOGIN ALPHA (XIGRIS®) PATIENT EVALUATION

Drotrecogin Alpha (activated) is recommended for patients with severe sepsis and acute organ dysfunction. It is recommended to be used on patients that meet the following inclusion criteria (sections 1, 2, and 3):

Inclusion Criteria 1: Patient has known or suspected infection defined as:

- A. Clinically important positive culture **OR**
- B. White cells in a normally sterile body fluid **OR**
- C. Perforated viscus **OR**
- D. Radiographic evidence of pneumonia in association with the production of purulent sputum.

- Meets
- Does not meet

Inclusion Criteria 2: Patient has three or more signs of SIRS (Systemic Inflammatory Response Syndrome) defined as:

- A. Core temperature greater than 38 degrees C or less than 36 degrees C
- B. Heart rate of greater than 90 beats/minute except in patients with a medical condition known to increase the heart rate or those receiving treatment that would prevent tachycardia.
- C. Respiratory rate greater than 20 breaths/minute or a PaCO₂ less than 32 mmg Hg or the use of mechanical ventilation for an acute respiratory process.
- D. White cell count of greater than 12,000/mm³ or less than 4,000/mm³ or a differential showing greater than 10% immature neutrophils.

- Meets
- Does not meet

Inclusion Criteria 3: Patient has at least one organ system dysfunction defined as:

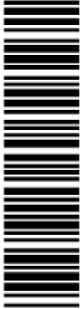
- A. Cardiovascular dysfunction: Arteriol systolic blood pressure less than 90 mm Hg or the mean arterial pressure less than 70 mm Hg for at least one hour despite adequate fluid resuscitation, adequate intravascular volume status or the use of vasopressors in an attempt to maintain a systolic blood pressure of greater than 90 mm Hg or a mean arterial pressure of greater than 70 mm Hg **OR**
- B. Kidney dysfunction: Urine output less than 0.5 ml/Kg. of body weight/hour for greater than one hour, despite adequate fluid resuscitation **OR**
- C. Respiratory dysfunction: Ratio of PaO₂ to FiO₂ less than 250 in the presence of other dysfunctional organs or systems or less than 200 if the lung was the only dysfunctional organ **OR**
- D. Hematologic dysfunction: Platelet count less than 80,000/mm³ or decreased by 50% in the 3 days preceding **OR**
- E. Unexplained metabolic acidosis: pH less than 7.3 or the base deficit greater than 5 mM/liter in association with a plasma lactate level that was greater than 1.5 times the upper limit of the normal value for the reporting laboratory.

- Meets
- Does not meet

Exclusion Criteria: If the patient meets **ANY** of the following exclusion criteria, treatment with Drotrecogin Alpha (activated) or Xigris® is **NOT** recommended.

- A. Active bleeding process **OR**
- B. Less than 3 months post hemorrhagic CVA, intracranial/spinal surgery, head trauma requiring hospitalization **OR**
- C. Any history of intracerebral arteriovenous malformation, cerebral aneurysm, or mass lesion of the central nervous system **OR**
- D. Less than 12 hours post surgery requiring general or spinal anesthesia **OR**
- E. Presence of an epidural catheter **OR**
- F. Trauma considered to increase the risk of bleeding

- Patient does not have any of the above conditions
- Patient has one or more of the above conditions



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DROTRECOGIN ALPHA (XIGRIS®) PATIENT EVALUATION

Specific Considerations: If the patient has no exclusion criteria, then patient specific considerations must be addressed. There is no safety and efficacy data in the following patient groups to support the use of Drotrecogin Alpha (activated).

- A. Platelet count less than 30,000/mm³
- B. Hereditary deficiency of Protein C, Protein S, or antithrombin III
- C. Gastrointestinal bleeding within 6 weeks before the study unless corrective surgery performed
- D. Less than 3 months from ischemic stroke
- E. Chronic renal failure requiring hemodialysis or peritoneal dialysis
- F. Known or suspected portosystemic hypertension, chronic jaundice/ascites or cirrhosis
- G. Use of the following medications or treatment regimens:
 - Unfractionated Heparin therapy > 15,000 units/24 hours
 - Direct thrombin inhibitors, e.g. Argatroban, Bivalirudin, Lepirudin
 - Low-molecular-weight Heparins at a higher dose than recommended prophylaxis
 - Warfarin therapy (if used within the past 7 days and INR exceeds upper limits of normal)
 - ASA at doses greater than 650 mg./day within the previous 3 days
 - NSAIDS, particularly long-acting products e.g. Ketoprofen ER
 - Anti-platelet agents, thrombolytics within the past 3 days, TPA, Retavase, Alteplase, Tenecteplase
 - Glycoprotein IIb/IIIa inhibitors within the previous 7 days, e.g. Integrilin® and Reopro®
 - Antithrombin III at a dose greater than 10,000 units within the past 12 hours
 - Protein C infusion within the last 24 hours
 - Other investigational agents known to affect coagulation
- H. Pregnancy and/or breast feeding
- I. Known hypercoagulable condition, including resistance to activated protein C
- J. Anticardiolipin antibody, antiphospholipid lupus anticoagulant, lupus anticoagulant, or homocystinemia
- K. Deep-vein thrombosis or pulmonary embolism, highly suspected or documented in previous 3 months
- L. Acute pancreatitis with no established source of infection
- M. Patients with HIV (CD⁴ less than 50)
- N. History of bone marrow or solid organ transplantation
- O. Age less than 18 years
- P. Weight greater than 135 Kg.

Evaluation Summary:

1. Patient must meet inclusion criteria 1, 2, and 3 for treatment consideration. (Severe Sepsis - 995.92)
 - Meets – Appropriate for treatment
 - Does not meet – Treatment not recommended
2. Patient meets exclusion criteria for which treatment is not recommended.
 - Meets – Treatment not recommended
 - Does not meet – Appropriate for treatment
3. The patient meets specific considerations, individualized evaluation is required prior to treatment consideration regardless of compliance to inclusion criteria.
 - Meets – Caution advised
 - Does not meet – Appropriate for treatment

Treatment Recommendation:

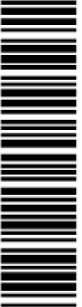
- Patient a candidate for Drotrecogin Alpha (activated) therapy (Infusion Xigris code 00.11 if given)
- Patient **NOT** a candidate for Drotrecogin Alpha (activated) therapy

Reference:

Adapted from the University Pharmacotherapy Associates 2001 Drotrecogin Patient Selection Consensus Guidelines for Drotrecogin.

Abbreviation Key

mm³ – cubic millimeter





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DROTRECIGIN ALPHA (ACTIVATED) - XIGRIS®

Patient Weight (Kg.) _____

Criteria:

Patient evaluation form must be completed. **All of the following must apply:**

- 1. Known or suspected infection (Inclusion criteria #1).
- 2. Three or more signs of SIRS (Systemic Inflammatory Response Syndrome) (Inclusion criteria #2).
- 3. Organ or system dysfunction (Inclusion criteria #3).
- No exclusion criteria met.
- Special considerations reviewed.

Infusion:

1. Drotrecogin Alpha (activated) - Xigris® 24 mcg./Kg./hr (_____ mcg./hr) IV in 0.9% NaCl for a total of 96 hours, start at _____ am/pm (please circle).
2. Discontinue Drotrecogin Alpha (activated) - Xigris® after 96 hours of infusion or for uncontrolled bleeding at any time.
3. Drotrecogin Alpha (activated) - Xigris® should be discontinued 2 hours prior to undergoing an invasive surgical procedure or procedures with an inherent risk of bleeding. Once adequate hemostasis has been achieved, initiation of Drotrecogin Alpha (activated) - Xigris® may be reconsidered 12 hours after major invasive procedures. Notify ordering physician before restarting infusion (peripheral venipuncture is allowed without interrupting infusion).
4. Notify pharmacy if infusion is interrupted for any reason.
5. Stop infusion 1 hour before any percutaneous procedure or minor surgery. In the absence of bleeding complications, may resume infusion one hour after percutaneous procedure or surgery. Notify pharmacy if infusion is interrupted for any reason.

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